Afwijking aan de inwendige organen bij pseudoxanthoma elasticum en angioide strepen

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SUMMARY

After a short introduction in the first chapter, the various clinical pictures of pseudoxanthoma elasticum are described. The most important feature of the microscopic picture is DARIER's so called "elastorhexis". The differential diagnosis from other skin-diseases has been dealt with extensively. Little is known yet about the aetiology and the pathogenesis of pseudoxanthoma elasticum. Various hypotheses in connection with this matter are discussed. Also about the genesis of the histopathological changes different opinions are held. In some recent publications the opinion has been expressed that, as a result of degenerative changes, in particular the collagen fibres have acquired the capacity to stain with elastin stains.

In the second chapter, after a short historical introduction, the ophthalmologic manifestations of angioid streaks are described. It appears from the literature that streaks may be completely absent, which goes to show that also in this respect the name angioid streaks is unfortunate. Several investigators found a fundus picture showing a patch- and dotdesign. ZEEMAN even spoke of "angioid streaks without angioid streaks". Others found only lesions of a central chorioretinitis. That we are still dealing with atypical manifestations of angioid streaks may be considered sufficiently proved by the simultaneous presence of pseudoxanthoma elasticum as well as by examination of relatives.

Afterwards the differential diagnosis of angioid streaks with other eye diseases is fully discussed. For a long time the pathogenesis of angioid streaks remained completely obscure. Only as late as 1938 - thanks to a histological examination of the eyeballs in two cases by HAGEDOORN and BÖCK - it was demonstrated with certainty, that angioid streaks are based upon primary degeneration of BRUCH's membrane which had been suggested first by KOFLER in 1917 and which, in 1929, was considered the most likely hypothesis by GRÖNBLAD because of the simultaneous occurrence of pseudoxanthoma elasticum in her patients. HAGEDOORN, BÖCK and later on KLIEN tried to explain the various aspects of angioid streaks by means of the most precise possible correlation of ophthalmoscopic and microscopic data. They found that these were not only determined by primary degeneration of BRUCH's membrane but also by sedundary changes in the tissues above and underneath this membrane.

According to the litterature the existance of PAGET's osteitis deformans may be expected in about 8% of the cases of angioid streaks. Not in a single case of PAGET's disease showing angioid streaks was pseudoxanthoma elasticum of the skin found simultaneously.

At the end of this chapter a possible connection between angioid streaks and trauma is discussed.

In the first part of the third chapter a few autopsy findings are described. Three of the six patients of whom a post-mortem examination was made (all of them were about 50 years old) died in coma, two of them as a result of encephalomalacia (cases PRICK

and URBACH) – the third as a result of intracranial hemorrhage (case KLIEN). The three other patients (cases VERHOEFF, TANNENHAIN and BALZER) died respectively of cardiac infarctions, profuse intestinal hemorrhage and advanced tuberculosis of the lungs. Only in two cases (PRICK and URBACH) had a sufficient histological examination – especially of vessels – been made. Thanks to these two autopsies and to the pathologico-anatomical examinations of a colloid struma removed by operation as well as to a biopsy of the ulnar artery, made during life, it could be established with certainty that in pseudoxanthoma elasticum and angioid streaks we are faced with a systemic disease. It is remarkable that in all these cases the changes caracteristic for pseudoxanthoma elasticum were found only in the media of the vessels, whilst degenerative lesions in the tunica elastica interna are absent. We believe that this fact and the observation that in the autopsies of PRICK and URBACH the elastic tissue of the lungs was completely intact, support the theory held by HANNAY and others, that pseudoxanthoma elasticum is based upon a degenerative proces of the collagenic connective tissue.

In the second part of the third chapter follows a systematic discussion of the internal manifestations which, according to the literature, may occur in cases of pseudoxanthoma elasticum and angioid streaks. It is pointed out that the majority of these internal disorders can be explained by anomalies of the vessels – whether or not complicated by arteriosclerosis. The survey of the literature shows that this systemic disease of the „elastic" tissue is often accompanied at an early stage by signs of mental, nervous and internal disturbances. Amongst the manifestations of internal disease angina pectoris, intermittent claudication hypertension and bleeding from various tracts are striking features. According to some investigators the same goes for thyrotoxicosis and diabetes, but we do not consider this sufficiently proved. Physical examination of these patients often shows a faint pulse and in the arteries of the legs a complete absence of the peripheral pulse. X ray-pictures have provided us with several cases – often at an early age – of dilatation and elongation of the aorta as well as peripheral calcification of the vessels. CARLBORG has shown by means of sphygmographic and oscillometric examinations that the peripheral vessels are abnormal in functional respect.

In the fourth chapter we deal with 20 new cases of angioid streaks and/or pseudoxanthoma elasticum, which we have studied ourselves. The youngest patient was 9 years of age, the oldest 84 years. They came from 14 different families. Several patients were brothers or sisters. In the cases no. IV, V and VI (three brothers), XIII and XV consanguinity of the parents existed. In 14 of the 20 cases the GRÖNBLAD-STRANDBERG syndrome – i.e. a combination of angioid streaks and pseudoxanthoma elasticum – could be observed. Microscopic examination showed in 4 of the 14 patients (no. II, III, X and XI) only minimal cutaneous lesions; histological examination however confirmed the clinical diagnosis. None of those 4 patients had noticed his skin-lesions himself, neither had the patients no. I, IV, V, VIII and XVIII, where the lesions were more obvious. Only 5 patients (no. VII, IX, XII,

XIII and XIV) were struck by the abnormal condition of their skin. Four of these consulted a doctor because of this „skin disease", the fifth (no. IX) did not consider this necessary, but his lesions were discovered during examination, when he was admitted to hospital because of gastric hemorrhage. Apart from these 14 cases showing a combination of angioid streaks and pseudoxanthoma elasticum there were 2 cases with fundus lesions (XIX and XX), that showed only microscopic cutaneous lesions. These two cases should also be classified with the GRÖNDBLAD-STRANDBERG syndrome, but they are recorded seperately in this survey, as the GRÖNBLAD-STRANDBERG cases mentioned in the literature always showed macroscopic skin lesions. In both these cases the pseudoxanthoma elasticum must be considered as an invisible dermatosis.

Summarizing we found a combination of angioid streaks and pseudoxanthoma elasticum in 16 patients. The four remaining cases showed the following peculiarities. In case no. VI we found a very early stage of angioid streaks without macroscopic and microscopic skin-lesions. Case no. VIII (a nine years old boy) had a pronounced pseudoxanthoma elasticum and bilateral macular lesions, but no angioid streaks. In case no. XVII, showing no angioid streaks but with macular changes of the left eye as they occur with angioid streaks, no macroscopic but only microscopic skin lesions were found viz. distinct „hyperplasia" of the elastic fibres without „elastorhexis". Case no. XVIII, an 84 year old woman, showed pseudoxanthoma elasticum and macular lesions, but no angioid streaks.

In 8 out of the 16 cases of angioid streaks mentioned the patients had a normal vision. All the same in 4 cases (VII, X, XII and XIV) slight pigmentary changes in the macular region could already be noticed. In cases no. IX and XVI several peripheral foci of „choroiditis" were observed, localised mainly along the angioid streaks. Moreover in case no. IX a pale right disc was found in association with a partial reduction of the visual field. With patient no. III vision of the left eye was normal, that of the right eye was 5/10 as the result of a (traumatic) rupture through the macula. The remaining seven patients showed medium to serious disturbances of vision, caused by central lesions. In case no. VIII an intense bilateral peripapillary atrophy was observed with a pronounced macular degeneration. In addition the pigment-streaks in this case show a peculiar segmented appearance as has been described by BEDELL among others. In the other six cases poor vision was caused by central choroiditis – or choroiretinitis lesions. These central choroiretinitis lesions should be considered as remnants of earlier subretinal exudates and/or hemorrhages. In a few patients (XV and XX) recent choroiditis lesions (XV and XX) and hemorrhages (I, XV and XX) were found. A strong early sclerosis of the choroid vessels was discovered in cases no. I, II, VIII, XV and XX.

Several of our patients had internal complaints. Fatigue, especially on physical exertion was repeatedly mentioned. General examination showed in 9 out of the 29 cases a strikingly faint radial pulse. Also the peripheral pulsation in the legs (a. dors. pedis and a. tibialis post.) was extremely faint, sometimes even completely absent. In several of these patients with a faint pulse

a loud second aortic sound with normal or only slightly increased bloodpressure was noticed. With most of these patients the bloodpressure was normal, in 5 cases only hypertension existed. An X ray examination showed an elongated aorta in 6 cases. In 2 cases a dilated aorta could be diagnosed with certainty. The heart of one patient, simultaneously suffering from angina pectoris, showed a marked enlargement to the left (aorta configuration). In this case also strong electrocardiographic deviations were found. The other patients did not show any deviation in the electrocardiogram. In 13 of the 20 cases the existence of peripheral calcification of the vessels was investigated. In 4 patients, 51, 52, 46 and 43 years of age respectively, this was established by means of X ray examination. In all these cases it was the arteries of the legs that showed calcification. In one case only was this also found in the arteries of the arms. Moreover in three patients X ray pictures of the skul showed calcification of the plexus, which PARNITZKE maintains is always pathological. Oscillometric and sphygmographic data have been gathered in tabel VIII and figures XIV, XV and XVI. Internal hemorrhage occurred in 4 of the 29 cases examined. The 3 patients in whom the eyespecialist observed recent hemorrhage of the fundus are not included. Patient no. IX suffered four times from a serious gastric hemorrhage, whilst an X ray picture failed to show an ulcer, and once from „spontaneous" haemarthrosis in the left knee; patient no. XII had a hemorrhage from the colon and patient no. XIV a few times a violent hemorrhage from the uterus. Patient no. XVI died in the age of 35 in coma, a subarachnoid hemorrhage being the most likely cause. As has been mentioned before, in 3 of the patients suffering from hemorrhage of the fundus no cause was found for the hemorrhage. Bleeding, coagulation and prothrombin times and thrombocyte counts were normal, whilst also the RUMPEL-LEEDE phenomenon was negative.

A neurologic-psychiatric examination was held in 8 cases. One patient (case no. III) showed the familial form of diplegia spastica infantilis. Patient no. XIX had mental debilitas, whilst 5 patients were affected by „slight defects of memory for recent events".

With 12 patients a more or less complete investigation of lung function was carried out. In 6 of these cases the residual air volume could be measured. It turned out to be normal in all cases, which according to most investigators is conclusive evidence against pulmonary emphysema. Neither did clinical or X ray examination provide any indication of pulmonary emphysema.

The maximum breathing volume (maximum minute ventilation) was established in ten cases. This volume and consequently also its relation to the about normal vital capacity was below normal in all cases but one. The one second value (given in % of the vital capacity) was established 8 times, four times being below normal. We cannot point out with certainty how these too low values (maximum breathing volume and one second value) are to be explained.

Examination of the voice took place in 5 cases. No changes in the voice, which might possibly indicate reduced elasticity of the vocal cords, were registred.

In the fifth chapter we hold the opinion that the hypothesis of those investigators who consider pseudoxanthoma elasticum as a systemic disease of the collagen and not of the elastic tissue, is the most probable one. Apart from their orceinophilia, the degenerated fibres show microscopically a marked resemblance to collagen fibres. Moreover the following arguments may be considered as indirect support for this hypothesis:

a) the intact condition of the tunica elastica interna, as described by various authors;
b) the normal histological picture of the elastic fibres of the lungs;
c) the absence (from a clinical point of view) of pulmonary emphysema in cases showing pseudoxanthoma elasticum and angioid streaks.